Search Paper 2

WEST Search History

DATE: Saturday, July 26, 2003

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L1	pre-eclampsia same inhibin	9	L1

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☐ 1. Document ID: US 20010055781 A1

L1: Entry 1 of 9 File: PGPB Dec 27, 2001

PGPUB-DOCUMENT-NUMBER: 20010055781
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010055781 A1

TITLE: Diagnosis of pre-eclampsia

PUBLICATION-DATE: December 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Groome, Nigel Patrick	Oxford		GB	
Knight, Philip Gerald	Reading		GB	
Ledger, William Leigh	Sheffield		GB	
Redman, Christopher Willard George	Oxford		GB	
Muttukrishna, Shanthi	Oxford		GB	

US-CL-CURRENT: 435/7.92

ABSTRACT:

A method for diagnosis of pre-eclampsia is disclosed, which comprises measuring the hormone inhibin A in a biological sample such as maternal serum. The method allows non-invasive, early diagnosis and can be used to predict the onset of secondary symptoms.

L1: Entry 1 of 9 File: PGPB Dec 27, 2001

DOCUMENT-IDENTIFIER: US 20010055781 A1
TITLE: Diagnosis of pre-eclampsia

Abstract Paragraph (1):
A method for diagnosis of pre-eclampsia is disclosed, which comprises measuring the hormone inhibin A in a biological sample such as maternal serum. The method allows non-invasive, early diagnosis and can be used to predict the onset of secondary symptoms.

Summary of Invention Paragraph (1):
[0001] This invention relates to detection of pre-eclampsia. In particular, it relates to early diagnosis of pre-eclampsia by detecting elevated levels of the hormone inhibin A.

Summary of Invention Paragraph (7):
[0007] It has now been discovered that the hormone inhibin A is significantly increased in cases of pre-eclampsia compared to normal pregnancies. Before secondary symptoms of pre-eclampsia are detectable, a group of patients who went on to develop pre-eclampsia showed a higher mean inhibin A level than a second group who did not go on to develop pre-eclampsia.

Summary of Invention Paragraph (8):
[0008] Inhibin A is a member of the family of inhibins which are heterodimeric proteins consisting of .alpha..beta..sub.A (inhibin A) and .alpha..beta..sub.B (inhibin B) subunits. The term "inhibin A" as used herein refers to the dimeric protein, which is the biologically active form of inhibin A. The two protein subunits are joined together by disulphide bonds. Inhibin A is produced mainly by the ovaries and has an endocrine role in inhibiting pituitary follicle stimulating hormone (FSH) production. In pregnancy, circulating levels of inhibin A are increased with the placenta being the major source (Muttukrishna et al 1995). In contrast, inhibin B levels are not elevated in either control or pre-eclampsia pregnancies.

Summary of Invention Paragraph (10):
[0010] It has also been discovered that maternal peripheral serum concentrations of the related hormones pro alpha C and activin A, when measured as total activin A, are significantly elevated in pre-eclampsia compared to normal maternal serum. Activins are homodimers consisting of .beta..sub.A.beta..sub.A (activin A), .beta..sub.A.beta..sub.B (activin AB) and .beta..sub.B.beta..sub.B (activin B) subunits linked by disulphide bridges. Activin A occurs naturally in free form and in bound form, bound to a protein called follistatin. "Total" activin A refers to both activin A whether free or bound. Pro alpha C is a part of the .alpha. subunit of inhibin A which is not present in the biologically active dimer. Serum human chorionic gonadotrophin (hCG) concentrations are also significantly higher in pre-eclampsia compared to normal pregnancy serum.

Summary of Invention Paragraph (12):
[0012] The present invention provides in one aspect a method of diagnosis of pre-eclampsia which method comprises measuring inhibin A in a biological sample.

Summary of Invention Paragraph (15):
[0015] In another aspect, the invention provides the use of inhibin A levels as an indicator of pre-eclampsia.

Summary of Invention Paragraph (16):
[0016] The invention may further comprise measuring the level of other proteins, which may be hormones and the use of other such proteins together with inhibin A as indicators of pre-eclampsia. The additional proteins measured may be one or more of the hormones activin A, pro alpha C and hCG. Where activin A is measured, this is preferably total activin A.

Summary of Invention Paragraph (18):
[0018] In yet another aspect, the invention provides the use of an antibody system specific for inhibin A in a test for pre-eclampsia.

Summary of Invention Paragraph (20):
[0020] In accordance with the present invention, it has been demonstrated that inhibin A levels are significantly increased in pre-eclamptic pregnancies over normal pregnancies. Not only that, it has also been found that there is no overlap in inhibin A levels between pre-eclamptic and normal pregnancies. Furthermore, it has been demonstrated that at an early stage in gestation, before the secondary symptoms of pre-eclampsia are normally detectable, a significantly higher inhibin A level is detectable in a group of patients who go on to develop pre-eclampsia compared to a control group of individuals who do not have a pre-eclamptic pregnancy.

Brief Description of Drawings Paragraph (4):
[0025] FIG. 3 shows a profile of inhibin A and activin A immunoreactivity after FPLC gel-permeation chromatography of control and pre-eclampsia maternal serum.

Brief Description of Drawings Paragraph (6):
[0027] FIG. 5 shows maternal serum inhibin A concentrations in individuals at 16 weeks gestation, for a group of patients who go on to develop pre-eclampsia and for a second group who do not develop pre-eclampsia.

Detail Description Paragraph (33):
[0059] Serial dilutions of control and pre-eclamptic serum gave response curves in the inhibin A (FIG. 1a), pro alpha C (FIG. 1c) and activin A (FIG. 1b) enzyme immunoassays which were parallel to that for the human recombinant inhibin A standard, human pro alpha C standard and human inhibin B standard respectively. Recovery of exogenous human recombinant inhibin A (3.8 pg/well), human recombinant activin A (100 pg/well) and pro alpha C (5 pg/well) added before assay to aliquots of control pregnancy serum (105.+-.6%, 113.+-.13%, 98.+-.3.2% respectively) and pre-eclampsia serum (94.9.+-.6.7%, 122.4.+-.19.2%, 105.+-.10.5% respectively) were almost quantitative.

Detail Description Paragraph (35):
[0061] Maternal serum concentrations of inhibin A (FIG. 2a) were increased by .about.8 fold (P<0.001) in pre-eclampsia compared to control pregnancies. Peripheral concentrations of pro alpha C (FIG. 2c) were almost 3 fold (P<0.001) enhanced and levels of activin A (FIG. 2b) were significantly (.about.9 fold, P<0.001) elevated in pre-eclampsia.

Detail Description Paragraph (41):
[0067] Measurement of serum inhibin A in samples taken at 16 weeks gestation indicates a significantly higher mean inhibin A concentration for a group of individuals who went on to suffer pre-eclampsia (327.+-.27.15 pg/ml), compared to a control group who did not develop pre-eclampsia (197.67.+-.23.77 pg/ml) (P=0.0097). Results are shown in FIG. 5.

Detail Description Paragraph (52):
[0077] FIG. 1 Parallel response curves for serial dilutions of protein standard, pooled control pregnancy serum and pooled pre-eclampsia serum in the (a) inhibin A, (b) activin A and (c) pro alpha C enzyme immunoassays. Values are means of duplicate determinations of absorbance.

Detail Description Paragraph (53):
[0078] FIG. 2 Scatter plot of individual concentrations of a) inhibin A, b) activin A, c) pro alpha C and d) hCG in maternal serum in pre-eclampsia (n=20) and control pregnancy (n=20).

Detail Description Paragraph (54):
[0079] FIG. 3 Profile of (a) inhibin A and (b) activin A immunoreactivity measured by EIA after FPLC gel-permeation chromatography of 100 .mu.l samples of control or pre-eclampsia maternal serum. Values are mean .+-.SEM (n=3 separate fractionations). The elution positions of the following proteins are indicated: .alpha..sub.2-macroglobulin (Vo; 725 kDa), alcohol dehydrogenase (AD; 150 kDa) bovine serum albumin (BSA; 66 kDa), recombinant human inhibin A (32 kDa), human recombinant activin A (24 kDa) and cytochrome C (12.5 kDa).

Detail Description Table CWU (1):
1TABLE 1 Gestational Gestation inhibin A activin A Pro alpha C hCG age (days) (weeks) parity (ng/ml) (ng/ml) (ng/ml) (IU/ml) PRE-ECLAMPSIA 206 29 0 + 0 1.26 10.97 0.67 33.79 187 27 0 + 0 >10 74.52 2.02 152.08 217 31 0 + 0 2.50 44.94 1.24 58.64 198 28 0 + 0 5.12 75.20 0.53 10.37 206 29 0 + 0 1.40 24.35 1.72 70.92 184 26 0 + 0 2.40 >100 0.57 57.34 229 33 0 + 0 2.07 19.38 1.50 35.26 191 27 0 + 0 5.15 51.43 0.71 27.85 173 25 0 + 0 5.45 39.10 1.70 98.71 233 33 0 + 0 5.48 33.30 0.96 47.82 Mean 3.43 41.47 1.16 59.28 SEM 0.61 7.57 0.18 13.63 165 24 1 + 1 1.58 17.55 2.14 18.38 205 29 0 + 0 0.93 30.04 1.90 129.17 249 36 1 + 0 6.08 20.68 3.50 91.49 191 27 0 + 0 1.17 14.73 1.96 56.87 212 30 0 + 0 2.12 101.98 1.88 12.22 153 22 1 + 0 2.01 18.58 1.76 52.55 239 34 0 + 0 2.10 27.93 2.39 131.56 183 26 1 + 3 4.19 37.37 2.64 16.56 228 33 2 + 0 3.76 57.80 1.69 40.76 236 34 0 + 1 3.22 23.64 2.11 38.68 Mean 2.72 35.03 2.20 58.82 SEM 0.50 8.44 0.17 14.01 Mean(n = 20) 3.05 38.08 1.68 59.05 SEM 0.38 5.46 0.17 9.28 CONTROL 213 30 0 + 0 0.37 7.22 0.47 33.23 198 28 0 + 0 0.54 3.49 0.49 23.25 208 30 0 + 0 0.31 4.37 0.44 18.06 193 28 0 + 0 0.34 4.39 0.53 16.79 210 30 0 + 0 0.47 5.23 1.05 18.38 191 27 0 + 0 0.26 3.51 0.36 15.37 230 33 0 + 0 0.54 3.59 0.83 33.40 196 28 0 + 0 0.29 1.53 0.39 20.24 181 26 0 + 0 0.47 1.74 0.31 5.57 225 32 0 + 0 0.53 7.36 0.98 7.44 Mean 0.41 4.24 0.58 19.18 SEM 0.03 0.62 0.08 2.91 159 23 2 + 0 0.13 1.47 11.80 205 29 0 + 0 0.29 1.95 0.52 23.36 250 36 1 + 0 0.39 4.56 0.94 7.83 197 28 0 + 0 0.25 1.38 0.55 17.06 223 32 0 + 0 0.28 9.85 0.64 8.37

142 20 1 + 0 0.11 1.71 16.72 244 35 0 + 0 0.63 3.76 1.12 23.16 194 28 2 + 0 0.32 3.64 0.67 9.27 216 31 1 + 0 0.21 4.05 6.38 223 32 0 + 0 0.41 4.19 0.53 10.19 Mean 0.30 3.66 0.71 13.41 SEM 0.05 0.79 0.07 1.98 Mean(n = 20) 0.36 3.95 0.63 16.30 SEM 0.03 0.49 0.06 1.84

CLAIMS:

1. A method of diagnosis of pre-eclampsia which method comprises measuring inhibin A in a biological sample.

6. The use of inhibin A levels as an indicator of pre-eclampsia.

7. The use of an antibody system specific for inhibin A in a test for pre-eclampsia.

☐ 2. Document ID: US 20010051341 A1

L1: Entry 2 of 9 File: PGPB Dec 13, 2001

PGPUB-DOCUMENT-NUMBER: 20010051341
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010051341 A1

TITLE: Non-invasive prenatal diagnosis

PUBLICATION-DATE: December 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lo, Yuk-Ming Dennis	Homantin		CN	
Wainscoat, James Stephen	Oxford		GB	

US-CL-CURRENT: 435/6; 435/440, 435/91.2, 435/91.5

ABSTRACT:

The invention relates to a detection method performed on a maternal serum or plasma from a pregnant female, which method comprises the presence of a nucleic acid of fetal origin in the sample. The invention enables non-invasive prenatal diagnosis including, for example, sex determination, blood typing and other genotyping, and detection of pre-eclampsia in the mother.

L1: Entry 2 of 9 File: PGPB Dec 13, 2001

DOCUMENT-IDENTIFIER: US 20010051341 A1
TITLE: Non-invasive prenatal diagnosis

Detail Description Paragraph (101):
[0122] Our data indicate that the concentration of fetal DNA is higher in pre-eclamptic compared with non-pre-eclamptic pregnancies. These results indicate that fetal DNA concentration measurement in maternal plasma may be used as a new marker for pre-eclampsia. Compared with other markers for pre-eclampsia, fetal DNA measurement is unique in that it is a genetic marker while other markers, such as activin A and inhibin A, are generally hormonal markers. By its nature, a test based on a genetic marker has the advantage that it is completely fetal specific.

☐ 3. Document ID: US 6492178 B1

L1: Entry 3 of 9 File: USPT Dec 10, 2002

US-PAT-NO: 6492178
DOCUMENT-IDENTIFIER: US 6492178 B1

TITLE: Methods of determining an increased risk of a woman carrying a downs syndrome affected fetus by measuring an analyte in a biological sample

DATE-ISSUED: December 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pandian; Murugan R.	Mission Viejo	CA		

US-CL-CURRENT: 436/65; 435/21, 435/4, 435/7.1, 435/7.4, 436/510, 436/814, 436/817, 436/818, 436/86, 436/87

ABSTRACT:

There are provided methods for assaying biological specimens for one or more of leptin, prorenin or renin in order to provide predictive information about the likelihood of a woman carrying a Downs Syndrome affected fetus.

16 Claims, 0 Drawing figures
Exemplary Claim Number: 1

L1: Entry 3 of 9 File: USPT Dec 10, 2002

DOCUMENT-IDENTIFIER: US 6492178 B1
TITLE: Methods of determining an increased risk of a woman carrying a downs syndrome affected fetus by measuring an analyte in a biological sample

Other Reference Publication (1):
Raty et al. , "Prediction of pre-eclampsia with maternal mid-trimester total renin, inhibin A, AFP and free. beta.-hCG levels." Prenatal Diagnosis, (1999) 19/2 (122-27)-abstract.*

☐ 4. Document ID: US 6258540 B1

L1: Entry 4 of 9 File: USPT Jul 10, 2001

US-PAT-NO: 6258540
DOCUMENT-IDENTIFIER: US 6258540 B1

TITLE: Non-invasive prenatal diagnosis

DATE-ISSUED: July 10, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lo; Yuk-Ming Dennis	Kowloon			CN
Wainscoat; James Stephen	Oxford			GB

US-CL-CURRENT: 435/6; 435/440, 435/91.2, 435/91.5

ABSTRACT:

The invention relates to a detection method performed on a maternal serum or plasma sample from a pregnant female, which method comprises detecting the presence of a nucleic acid of foetal origin in the sample. The invention enables non-invasive prenatal diagnosis including for example sex determination, blood typing and other genotyping, and detection of pre-eclampsia in the mother.

27 Claims, 16 Drawing figures
Exemplary Claim Number: 1,25
Number of Drawing Sheets: 4

L1: Entry 4 of 9 File: USPT Jul 10, 2001

DOCUMENT-IDENTIFIER: US 6258540 B1
TITLE: Non-invasive prenatal diagnosis

Detailed Description Text (101):
Our data indicate that the concentration of foetal DNA is higher in pre-eclamptic compared with non-pre-eclamptic pregnancies. These results indicate that foetal DNA concentration measurement in maternal plasma may be used as a new marker for pre-eclampsia. Compared with other markers for pre-eclampsia, foetal DNA measurement is unique in that it is a genetic marker while other markers, such as activin A and inhibin A, are generally hormonal markers. By its nature, a test based on a genetic marker has the advantage that it is completely foetal-specific.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments
KWIC | Draw Desc | Image

☐ 5. Document ID: WO 9964860 A2

L1: Entry 5 of 9 File: EPAB Dec 16, 1999

PUB-NO: WO009964860A2
DOCUMENT-IDENTIFIER: WO 9964860 A2
TITLE: PREDICTIVE TEST FOR PRE-ECLAMPSIA

PUBN-DATE: December 16, 1999

INVENTOR-INFORMATION:

NAME	COUNTRY
WALD, NICHOLAS JOHN	GB
REDMAN, CHRISTOPHER	GB

INT-CL (IPC): G01 N 33/50
EUR-CL (EPC): G01N033/76

ABSTRACT:

CHG DATE=20000202 STATUS=O>A method is provided which enables a prediction to be made about the risk of a pregnant woman developing pre-eclampsia which comprises an analysis of the serum levels of screening markers, Inhibin A and free beta -hCG. Apparatus for carrying out the determination of the risk of developing pre-eclampsia

based on the analysis of the serum samples is also provided.

L1: Entry 5 of 9 File: EPAB Dec 16, 1999

DOCUMENT-IDENTIFIER: WO 9964860 A2
TITLE: PREDICTIVE TEST FOR PRE-ECLAMPSIA

Abstract Text (1):
CHG DATE=20000202 STATUS=O>A method is provided which enables a prediction to be made about the risk of a pregnant woman developing pre-eclampsia which comprises an analysis of the serum levels of screening markers, Inhibin A and free beta -hCG. Apparatus for carrying out the determination of the risk of developing pre-eclampsia based on the analysis of the serum samples is also provided.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 6. Document ID: WO 9802751 A1

L1: Entry 6 of 9 File: EPAB Jan 22, 1998

PUB-NO: WO009802751A1
DOCUMENT-IDENTIFIER: WO 9802751 A1
TITLE: DIAGNOSIS OF PRE-ECLAMPSIA

PUBN-DATE: January 22, 1998

INVENTOR-INFORMATION:

NAME	COUNTRY
GROOME, NIGEL PATRICK	GB
KNIGHT, PHILIP GERALD	GB
LEDGER, WILLIAM LEIGH	GB
REDMAN, CHRISTOPHER WILLARD GEO	GB
MUTTUKRISHNA, SHANTHI	GB

INT-CL (IPC): G01 N 33/74
EUR-CL (EPC): G01N033/74

ABSTRACT:

CHG DATE=19990617 STATUS=O>A method for diagnosis of pre-eclampsia is disclosed, which comprises measuring the hormone inhibin A in a biological sample such as maternal serum. The method allows non-invasive, early diagnosis and can be used to predict the onset of secondary symptoms.

L1: Entry 6 of 9 File: EPAB Jan 22, 1998

DOCUMENT-IDENTIFIER: WO 9802751 A1
TITLE: DIAGNOSIS OF PRE-ECLAMPSIA

Abstract Text (1):
CHG DATE=19990617 STATUS=O>A method for diagnosis of pre-eclampsia is disclosed, which comprises measuring the hormone inhibin A in a biological sample such as maternal serum. The method allows non-invasive, early diagnosis and can be used to predict the onset of secondary symptoms.

☐ 7. Document ID: WO 9964860 A2 AU 9942802 A EP 1084412 A2 JP 2002517755 W AU 751415 B

L1: Entry 7 of 9 File: DWPI Dec 16, 1999

DERWENT-ACC-NO: 2000-116596
DERWENT-WEEK: 200271

TITLE: Predicting the risk of pre-eclampsia in a pregnant woman comprises analyzing a blood sample for free beta-human chorionic gonadotrophin and inhibin A

INVENTOR: REDMAN, C; WALD, N J

PRIORITY-DATA: 1998GB-0012432 (June 9, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9964860 A2	December 16, 1999	E	032	G01N033/50
AU 9942802 A	December 30, 1999		000	G01N033/50
EP 1084412 A2	March 21, 2001	E	000	G01N033/76
JP 2002517755 W	June 18, 2002		037	G01N033/53
AU 751415 B	August 15, 2002		000	G01N033/50

INT-CL (IPC): G01 N 33/50; G01 N 33/53; G01 N 33/68; G01 N 33/74; G01 N 33/76

ABSTRACTED-PUB-NO: WO 9964860A
BASIC-ABSTRACT:

NOVELTY - Predicting the risk of pre-eclampsia in a pregnant woman, comprises:

(a) obtaining a sample of blood from the woman;

(b) assaying the sample for the levels of free beta -human chorionic gonadotrophin (free beta -HCG) and Inhibin A present in the sample; and

(c) determining the risk of pre-eclampsia using the measured levels of free beta -HCG) and Inhibin A present in the sample.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an apparatus for determining whether a pregnant woman is at an increased risk of pre-eclampsia, the apparatus comprising: (a) data input means for inputting a measurement of the serum levels of Inhibin A and free beta -HCG in a sample obtained from the pregnant woman; and (b) calculation means for determining the risk of pre-eclampsia using the input levels of the serum markers Inhibin A and free beta -hCG; and

(2) a kit for predicting the onset of pre-eclampsia in a pregnant woman, comprising means for assaying a sample from the women for the levels of free beta -HCG and Inhibin A present in the sample.

USE - For predicting the risk of pre-eclampsia in a pregnant woman.

ADVANTAGE - Provides an improved level of predictiveness over previously known tests.

L1: Entry 7 of 9 File: DWPI Dec 16, 1999

DERWENT-ACC-NO: 2000-116596
DERWENT-WEEK: 200271

TITLE: Predicting the risk of pre-eclampsia in a pregnant woman comprises analyzing a blood sample for free beta-human chorionic gonadotrophin and inhibin A

Basic Abstract Text (4):
(c) determining the risk of pre-eclampsia using the measured levels of free beta -HCG) and Inhibin A present in the sample.

Basic Abstract Text (6):
(1) an apparatus for determining whether a pregnant woman is at an increased risk of pre-eclampsia, the apparatus comprising: (a) data input means for inputting a measurement of the serum levels of Inhibin A and free beta -HCG in a sample obtained from the pregnant woman; and (b) calculation means for determining the risk of pre-eclampsia using the input levels of the serum markers Inhibin A and free beta -hCG; and

Basic Abstract Text (7):
(2) a kit for predicting the onset of pre-eclampsia in a pregnant woman, comprising means for assaying a sample from the women for the levels of free beta -HCG and Inhibin A present in the sample.

☐ 8. Document ID: WO 9960020 A1 JP 2002515234 W AU 9941899 A EP 1080106 A1

L1: Entry 8 of 9 File: DWPI Nov 25, 1999

DERWENT-ACC-NO: 2000-116311
DERWENT-WEEK: 200238

TITLE: New polynucleotides encoding secreted cDNA libraries, used to develop products for the diagnosis and treatment of neoplastic disease

INVENTOR: COLLINS-RACIE, L A; EVANS, C ; JACOBS, K ; LAVALLIE, E R ; MCCOY, J M ; MERBERG, D ; MI, S ; TREACY, M

PRIORITY-DATA: 1998US-0175928 (October 20, 1998), 1998US-0080478 (May 18, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9960020 A1	November 25, 1999	E	149	C07K014/00
JP 2002515234 W	May 28, 2002		172	C12N015/09
AU 9941899 A	December 6, 1999		000	C07K014/00
EP 1080106 A1	March 7, 2001	E	000	C07K014/00

INT-CL (IPC): A61 K 38/00; A61 K 45/00; A61 K 48/00; A61 P 7/00; A61 P 17/02; A61 P 29/00; A61 P 35/00; A61 P 37/02; A61 P 43/00; C07 K 7/00; C07 K 14/00; C07 K 14/47; C12 N 5/10; C12 N 15/09; C12 N 15/11; C12 N 15/12; C12 N 15/63; C12 P 21/02; C12 Q 1/02; C12 Q 1/68

ABSTRACTED-PUB-NO: WO 9960020A
BASIC-ABSTRACT:

NOVELTY - New secreted proteins are encoded by polynucleotides obtained from human adult testes, human adult placenta, human adult brain, human adult blood, murine adult bone marrow, and murine adult thymus cDNA libraries.

DETAILED DESCRIPTION - New isolated polynucleotides (PNs) comprise:

(a) one of the defined sequences (S1)-(S7) of 2166, 2946, 3153, 2426, 271, 1630, 1351 nucleotides (nt), respectively (all given in the specification) or specified fragments of these defined as follows:

(a) comprising nt 44-1204 or 1-403 of (S1);

(b) 928-2541, 988-2541, or 684-1128 of (S2);

(c) 6-2408 or 1295-1705 of (S3);

(d) 2113-2337 or 2036-2316 of (S4);

(e) 144-257 or 30-271 of (S5);

(f) 431-520 or 266-511 of (S6), and

(g) 218-1159, 806-1159 or 217-517 of (S7);

(b) nt sequence (NS) of the full-length protein-coding sequence of clones AJ263, AJ1722, BL8913, BL3414, CC2517, CC39719, and D3052, G551, K4831, (clones deposited as ATCC 98115 or 98153);

(c) a sequence encoding either the full-length or the mature protein or species homolog encoded by the cDNA insert of the above clones

(d) a sequence encoding a protein comprising one of the sequences (S1')-(S7') of 387, 538, 800, 75, 38, 30, and 314 amino acids (aa) (all given in the specification) or fragments having biological activity, and

(e) allelic variants and PNs able to hybridize to any of the above under stringent conditions.

INDEPENDENT CLAIMS are also included for the following:

(1) proteins comprising:

(a) an aa sequence encoded by the cDNA insert of one of the above clones; or

(b) sequences (S1')-(S7') or their fragments comprising as follows:

(i) aa 1-120 of (S1');

(ii) aa 1-67 of (S2');

(iii) aa 431-567 of (S3');

(iv) aa 1-68 of (S4');

(v) aa 1-27 of (S6');

(vi) aa 1-100 of (S7');

(2) an isolated gene corresponding to a cDNA sequence (S1)-(S7), 338 (S8), 387 (S9) and 348 (S10) bp (given in the specification);

(3) a PN of sequence (1) operably linked to an expression control sequence;

(4) a host cell transformed with a composition as in (3);

(5) promoting cell-cell fusion comprising contacting a first cell and a second cell, where the first cell expresses an AJ1722 protein;

(6) inhibiting cell-cell fusion between a first cell which expresses an AJ1722 protein and a second cell, comprising contacting the first cell with an AJ1722 protein antagonist;

(7) inhibiting blastocyst implantation comprising contacting a cell within the blastocyst which expresses an AJ1722 protein with an AJ1722 antagonist;

(8) inhibiting trophoblast invasion comprising contacting a first cell which expresses an AJ1722 protein with an AJ1722 protein antagonist;

(9) diagnosing or predicting the existence of a condition associated with disregulation of AH1722 protein in a mammalian subject comprising:

(a) determining a first level of expression of AJ1722 protein in the subject; and

(b) comparing the first level of expression to a second level of expression of AJ1722 protein in one or more other mammalian subjects which do not have the condition;

(10) treating a neoplastic disease in a mammalian subject comprising administering to the subject an agent which modulated the expression or function of AJ1722, and

(11) inhibiting metastasis in a mammalian subject comprising administering an agent which modulates the expression or function of AJ1722;

USE - The PNs and proteins are predicted to have biological activities which would make them suitable for treating, preventing or ameliorating medical conditions in humans and animals. Detection of AH1722 protein levels can be used for the diagnosis of e.g. pre-eclampsia, placental pathology or cancer (claimed). Agents which modulate the expression or function of AJ1822 can be used for treating a neoplastic disease and inhibiting metastasis (claimed). Other suggested activities include nutritional activity (e.g. in feeds), cytokine and cell proliferation/differentiation activity, immune stimulating (e.g. as vaccines) or suppressing activity, hematopoiesis regulating activity, tissue growth activity, activin/inhibin activity, chemotactic/chemokineti c activity, hemostatic and thrombolytic activity, receptor/ligand activity, anti-inflammatory activity, cadherin/tumor invasion suppressor activity, and tumor inhibition activity. The PNs are also stated to be useful for gene therapy.

L1: Entry 8 of 9 File: DWPI Nov 25, 1999

DERWENT-ACC-NO: 2000-116311
DERWENT-WEEK: 200238

TITLE: New polynucleotides encoding secreted cDNA libraries, used to develop products for the diagnosis and treatment of neoplastic disease

Basic Abstract Text (37):
USE - The PNs and proteins are predicted to have biological activities which would make them suitable for treating, preventing or ameliorating medical conditions in humans and animals. Detection of AH1722 protein levels can be used for the diagnosis of e.g. pre-eclampsia, placental pathology or cancer (claimed). Agents which modulate the expression or function of AJ1822 can be used for treating a neoplastic disease and inhibiting metastasis (claimed). Other suggested activities include nutritional activity (e.g. in feeds), cytokine and cell proliferation/differentiation activity, immune stimulating (e.g. as vaccines) or suppressing activity, hematopoiesis regulating activity, tissue growth activity, activin/inhibin activity, chemotactic/chemokineti c activity, hemostatic and thrombolytic activity, receptor/ligand activity, anti-inflammatory activity, cadherin/tumor invasion suppressor activity, and tumor inhibition activity. The PNs are also stated to be useful for gene therapy.

☐ 9. Document ID: ES 2177989 T3 WO 9802751 A1 EP 927355 A1 US 20010055781 A1 EP 927355 B1 DE 69712899 E

L1: Entry 9 of 9 File: DWPI Dec 16, 2002

DERWENT-ACC-NO: 1998-110748
DERWENT-WEEK: 200306

TITLE: Diagnosing pre-eclampsia by measuring inhibin A in biological samples - provides indicator or allows prediction of pre-eclampsia, useful for early screening prior to symptom development

INVENTOR: GROOME, N P; KNIGHT, P G ; LEDGER, W L ; MUTTUKRISHNA, S ; REDMAN, C W G

PRIORITY-DATA: 1996GB-0014615 (July 11, 1996)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
ES 2177989 T3	December 16, 2002		000	G01N033/74
WO 9802751 A1	January 22, 1998	E	025	G01N033/74
EP 927355 A1	July 7, 1999	E	000	G01N033/74
US 20010055781 A1	December 27, 2001		000	G01N033/53
EP 927355 B1	May 29, 2002	E	000	G01N033/74
DE 69712899 E	July 4, 2002		000	G01N033/74

INT-CL (IPC): G01 N 33/53; G01 N 33/537; G01 N 33/543; G01 N 33/74

ABSTRACTED-PUB-NO: EP 927355B
BASIC-ABSTRACT:

Diagnosing pre-eclampsia comprises measuring inhibin A in a biological sample. Also claimed are: (1) The use of inhibin A levels as an indicator of pre-eclampsia; (2) the use of an antibody system specific for inhibin A in a test for pre-eclampsia.

USE - The method can be used to predict pre-eclampsia (i.e. predict that the characteristic secondary symptoms e.g. high blood pressure, oedema, proteinuria etc. will occur), or to indicate its presence (claimed). Pre-eclampsia is a multisystem disease of pregnancy of unknown cause, occurring in approximately one in ten pregnant women and, in severe cases (approximately 10 %), increasing the risk of early delivery and endangering the lives of babies and mothers. Using the method, it is possible to detect pre-eclampsia prior to symptom development (which normally occurs from 28 weeks) making it possible to intervene in affected pregnancies e.g. by treating with anti-hypersensitive drugs, increased monitoring and foetal surveillance, monitoring of placental function etc. Foetal and maternal outcome may thus be improved, and pregnancy prolonged safely to reduce prematurity, one of the main causes of foetal mortality and neonatal and childhood handicap.

ADVANTAGE - The method allows non-invasive, early diagnosis prior to symptom development, enabling screening for the disease not previously possible.
ABSTRACTED-PUB-NO:

US20010055781A EQUIVALENT-ABSTRACTS:

Diagnosing pre-eclampsia comprises measuring inhibin A in a biological sample. Also claimed are: (1) The use of inhibin A levels as an indicator of pre-eclampsia; (2) the use of an antibody system specific for inhibin A in a test for pre-eclampsia.

USE - The method can be used to predict pre-eclampsia (i.e. predict that the characteristic secondary symptoms e.g. high blood pressure, oedema, proteinuria etc. will occur), or to indicate its presence (claimed). Pre-eclampsia is a multisystem disease of pregnancy of unknown cause, occurring in approximately one in ten pregnant women and, in severe cases (approximately 10 %), increasing the risk of early delivery and endangering the lives of babies and mothers. Using the method, it is possible to detect pre-eclampsia prior to symptom development (which normally occurs from 28 weeks) making it possible to intervene in affected pregnancies e.g. by treating with anti-hypersensitive drugs, increased monitoring and foetal surveillance, monitoring of placental function etc. Foetal and maternal outcome may thus be improved, and pregnancy prolonged safely to reduce prematurity, one of the main causes of foetal mortality and neonatal and childhood handicap.

ADVANTAGE - The method allows non-invasive, early diagnosis prior to symptom development, enabling screening for the disease not previously possible.

Diagnosing pre-eclampsia comprises measuring inhibin A in a biological sample. Also claimed are: (1) The use of inhibin A levels as an indicator of pre-eclampsia; (2) the use of an antibody system specific for inhibin A in a test for pre-eclampsia.

USE - The method can be used to predict pre-eclampsia (i.e. predict that the characteristic secondary symptoms e.g. high blood pressure, oedema, proteinuria etc. will occur), or to indicate its presence (claimed). Pre-eclampsia is a multisystem disease of pregnancy of unknown cause, occurring in approximately one in ten pregnant women and, in severe cases (approximately 10 %), increasing the risk of early delivery and endangering the lives of babies and mothers. Using the method, it is possible to detect pre-eclampsia prior to symptom development (which normally occurs from 28 weeks) making it possible to intervene in affected pregnancies e.g. by treating with anti-hypersensitive drugs, increased monitoring and foetal surveillance, monitoring of placental function etc. Foetal and maternal outcome may thus be improved, and pregnancy prolonged safely to reduce prematurity, one of the main causes of foetal mortality and neonatal and childhood handicap.

ADVANTAGE - The method allows non-invasive, early diagnosis prior to symptom development, enabling screening for the disease not previously possible.

WO 9802751A

L1: Entry 9 of 9 File: DWPI Dec 16, 2002

DERWENT-ACC-NO: 1998-110748
DERWENT-WEEK: 200306

TITLE: Diagnosing pre-eclampsia by measuring inhibin A in biological samples - provides indicator or allows prediction of pre-eclampsia, useful for early screening prior to symptom development

Basic Abstract Text (1):
Diagnosing pre-eclampsia comprises measuring inhibin A in a biological sample. Also claimed are: (1) The use of inhibin A levels as an indicator of pre-eclampsia; (2) the use of an antibody system specific for inhibin A in a test for pre-eclampsia.

Equivalent Abstract Text (1):
Diagnosing pre-eclampsia comprises measuring inhibin A in a biological sample. Also claimed are: (1) The use of inhibin A levels as an indicator of pre-eclampsia; (2) the use of an antibody system specific for inhibin A in a test for pre-eclampsia.

Equivalent Abstract Text (4):
Diagnosing pre-eclampsia comprises measuring inhibin A in a biological sample. Also claimed are: (1) The use of inhibin A levels as an indicator of pre-eclampsia; (2) the use of an antibody system specific for inhibin A in a test for pre-eclampsia.

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PRE-ECLAMPSIA	488
PRE-ECLAMPSIUM	0
PRE-ECLAMPSIUMS	0
PRE-ECLAMPSIAS	1
INHIBIN	1635
INHIBINS	538
(PRE-ECLAMPSIA SAME INHIBIN).USPT,PGPB,JPAB,EPAB,DWPI.	9
(PRE-ECLAMPSIA SAME INHIBIN).USPT,PGPB,JPAB,EPAB,DWPI.	9

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Search Paper 12

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 NEWS  3  Feb 24    PCTGEN now available on STN
 NEWS  4  Feb 24    TEMA now available on STN
 NEWS  5  Feb 26    NTIS now allows simultaneous left and right truncation
 NEWS  6  Feb 26    PCTFULL now contains images
 NEWS  7  Mar 04    SDI PACKAGE for monthly delivery of multifile SDI results
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                    structures available in REGISTRY
 NEWS 10  Apr 11    Display formats in DGENE enhanced
 NEWS 11  Apr 14    MEDLINE Reload
 NEWS 12  Apr 17    Polymer searching in REGISTRY enhanced
 NEWS 13  Jun 13    Indexing from 1947 to 1956 added to records in CA/CAPLUS
 NEWS 14  Apr 21    New current-awareness alert (SDI) frequency in
                    WPIDS/WPINDEX/WPIX
 NEWS 15  Apr 28    RDISCLOSURE now available on STN
 NEWS 16  May 05    Pharmacokinetic information and systematic chemical names
                    added to PHAR
 NEWS 17  May 15    MEDLINE file segment of TOXCENTER reloaded
 NEWS 18  May 15    Supporter information for ENCOMPPAT and ENCOMPLIT updated
 NEWS 19  May 19    Simultaneous left and right truncation added to WSCA
 NEWS 20  May 19    RAPRA enhanced with new search field, simultaneous left and
                    right truncation
 NEWS 21  Jun 06    Simultaneous left and right truncation added to CBNB
 NEWS 22  Jun 06    PASCAL enhanced with additional data
 NEWS 23  Jun 20    2003 edition of the FSTA Thesaurus is now available
 NEWS 24  Jun 25    HSDB has been reloaded
 NEWS 25  Jul 16    Data from 1960-1976 added to RDISCLOSURE
 NEWS 26  Jul 21    Identification of STN records implemented
 NEWS 27  Jul 21    Polymer class term count added to REGISTRY
 NEWS 28  Jul 22    INPADOC: Basic index (/BI) enhanced; Simultaneous Left and
                    Right Truncation available

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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=> s pre-eclampsia
L1        12735 PRE-ECLAMPSIA

=> s l1 and inhibin and (hcg or human chorionic gonadotrophin) and oestriol
L2            0 L1 AND INHIBIN AND (HCG OR HUMAN CHORIONIC GONADOTROPHIN) AND
                OESTRIOL

=> s pre-eclampsia and diagnos?
L3         2638 PRE-ECLAMPSIA AND DIAGNOS?

=> s l3 and inhibin
L4           30 L3 AND INHIBIN

=> s l4 and oestriol
L5            0 L4 AND OESTRIOL

=> s l3 and review/dt
L6          304 L3 AND REVIEW/DT

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L7           304 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)

=> s l7 and py<1999
L8          192 L7 AND PY<1999

=> d 1-10 bib ab

L8   ANSWER 1 OF 192      MEDLINE on STN
AN   2000489735      MEDLINE
DN   20493879    PubMed ID: 11038861
TI   Progress in the study of perinatology in China.
AU   Bian X
SO   CHUNG-HUA I HSUEH TSA CHIH [CHINESE MEDICAL JOURNAL], (1998 Dec)
     78 (12) 918.  Ref: 0
     Journal code: 7511141. ISSN: 0376-2491.
CY   China
DT   Journal; Article; (JOURNAL ARTICLE)
       General Review; (REVIEW)
     (REVIEW, TUTORIAL)
LA   Chinese
FS   Priority Journals
EM   200101
ED   Entered STN: 20010322
     Last Updated on STN: 20010322
     Entered Medline: 20010111

L8   ANSWER 2 OF 192      MEDLINE on STN
AN   1999262329      MEDLINE
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DN 99262329 PubMed ID: 10325528
TI [Prediction of preeclampsia:new hypotheses, new approaches]. Pradiktion der Praeklampsie: neue Hypothesen, neue Ansatze.
AU Muller H M; Widschwendter M; Mortl M G; Schrocksnadel H
CS Universitatsklinik fur Gynakologie und Geburtshilfe, Innsbruck, Osterreich.. hannes.mueller@uibk.ac.at
SO GYNAKOLOGISCH-GEBURTSHILFLICHE RUNDSCHAU, **(1998)** 38 (4) 222-31.
Ref: 81
Journal code: 9212667. ISSN: 1018-8843.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals
EM 199907
ED Entered STN: 19990715
Last Updated on STN: 19990715
Entered Medline: 19990707
AB Preeclampsia is a multisystem disorder affecting 5.8% of primigravidas. It is a progressive disease with a very variable mode of presentation and rate of progression. Of all the features of the syndrome, hypertension and pregnancy-induced proteinuria are the classic clinical manifestations. This disease causes severe complications of the mother and the fetus. Neither are factors available for prediction, nor are there strategies for prevention and therapy of this disease. The accumulated evidence strongly suggests that failure or incomplete trophoblastic invasion (end of first, beginning of second trimester) of the spiral arteries, resulting in narrowed spiral arteries and subsequent endothelial damage, is responsible for the occurrence of this disease (third trimester). The reason for trophoblastic failure is not known. After clinical symptoms have occurred, only symptomatic therapeutic options are available. In this paper, we discuss potential ways to find specific and sensitive predictive parameters according to the current knowledge of the pathophysiology of this pregnancy-induced severe disorder.

L8 ANSWER 3 OF 192 MEDLINE on STN
AN 1999201653 MEDLINE
DN 99201653 PubMed ID: 10101437
TI **Pre-eclampsia**/eclampsia: a literature review.
AU Sungani F C; Malata A; Masanjika R
CS Department of Obstetrics and Gynaecology, College of Medicine, University of Malawi.
SO CENTRAL AFRICAN JOURNAL OF MEDICINE, **(1998 Oct)** 44 (10) 261-3.
Ref: 10
Journal code: 0372566. ISSN: 0008-9176.
CY Zimbabwe
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199904
ED Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990415
AB A review of literature on **pre-eclampsia**/eclampsia indicates that this is one of the commonest causes of high maternal and infant mortality and morbidity rates. Current information on the condition indicates that use of aspirin, phenytoin and magnesium sulphate are on the increase. However, in Malawi lytic cocktail and use of antihypertensives such as Hydralazine and, anticonvulsants such as Valium are currently in use. Even with this type of management, Malawi experiences high morbidity and mortality rates. This literature review

was done to identify baseline data for a study to be carried out in some of the hospitals in Malawi to establish a protocol for effective management of **pre-eclampsia** and eclampsia in Malawi.
It is hoped that after using low dose aspirin and magnesium sulphate, the morbidity and mortality caused by the disease will be reversed with time.

L8 ANSWER 4 OF 192 MEDLINE on STN
AN 1999129154 MEDLINE
DN 99129154 PubMed ID: 9930293
TI Obstetric management of high-order multiple pregnancies.
AU Newman R B
CS Department of Obstetrics and Gynecology, Medical University of South Carolina, Charleston 29425-2233, USA.
SO BAILLIERES CLINICAL OBSTETRICS AND GYNAECOLOGY, **(1998 Mar)** 12 (1) 109-29. Ref: 84
Journal code: 8710782. ISSN: 0950-3552.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990301
Last Updated on STN: 19990301
Entered Medline: 19990218
AB High-order multiples are increasingly common as a result of assisted reproductive technologies and represent pregnancies at exceptional risk. This article discusses the antepartum management of high-order multiples, which has in general been highly individualized and poorly studied. Care for high-order multiples should include preterm birth prevention education, the frequent assessment of maternal symptoms and cervical status by a consistent provider, individualized modification of activity, attention to maternal nutrition, ultrasonography for the assessment of fetal anatomy and intra-uterine growth and anticipation of maternal complications. Interventions such as prophylactic cerclage, uterine activity monitoring, prophylactic tocolysis or hospitalization have not improved outcome when used routinely, and guidelines for selective use will be presented. Specialized care for high-order multiples should be directed at identifying congenital anomalies, maximizing fetal growth and preventing early preterm birth, the effect of which will be to improve perinatal outcome for these exceptional pregnancies.

L8 ANSWER 5 OF 192 MEDLINE on STN
AN 1999099522 MEDLINE
DN 99099522 PubMed ID: 9883069
TI [Arterial hypertension and pregnancy: **diagnostic** criteria and therapeutic approach].
Hipertension arterial y embarazo: criterios **diagnosticos** y enfoque terapeutico.
AU Palma Gamiz J L
CS Servicio de Cardiologia, Hospital Ramon y Cajal, Madrid.
SO REVISTA ESPANOLA DE CARDIOLOGIA, **(1998)** 51 Suppl 4 50-8. Ref: 34
Journal code: 0404277. ISSN: 0300-8932.
CY Spain
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Spanish
FS Priority Journals
EM 199901
ED Entered STN: 19990209
Last Updated on STN: 19990209

Entered Medline: 19990128

AB Arterial hypertension is a relatively common complication of pregnancy, affecting about 10% of all normal pregnancies. The American College of Obstetric and Gynecology established in 1972 four different forms of arterial hypertension during pregnancy: a) arterial hypertension related to pregnancy, the so-called **pre-eclampsia**; b) arterial hypertension unrelated to pregnancy or chronic arterial hypertension; c) **Pre-eclampsia** superimposed on chronic arterial hypertension, and d) Transient or late arterial hypertension (third trimester). **Pre-eclampsia** and arterial hypertension are two different illnesses with different approaches and treatments. The mechanisms involved in arterial hypertension and **pre-eclampsia** of pregnant women are presently very well known, including genetic causes, alterations on the renin-angiotensin system, imbalance between vasoconstrictor and vasodilator agents derived from endothelial activity of the spiral arteries of the placenta, such as; prostacyclins, thromboxane A2, nitric oxide, endothelin-1, etc. The placenta is the key factor in inducing **pre-eclampsia**, and its expulsion during delivery or cesarean section is the definite cure of the process. All hypertensive forms during pregnancy increase the risks on both the mother and the fetus. Maternal risk is based on renal, metabolic and haematologic disorders, leading in some cases to cerebral haemorrhage or hepatic rupture. In the fetus, **pre-eclampsia** significantly increases the risk of still-birth, abruptio placentae, hypocalvaria, intrauterine growth retardation, and prematurity. Clinical, biochemical and haematologic manifestations of **pre-eclampsia** are very typical, facilitating an early and easy **diagnosis**.

L8 ANSWER 6 OF 192 MEDLINE on STN
AN 1999067515 MEDLINE
DN 99067515 PubMed ID: 9850529
TI 1998 update on pregnancy in lupus patients. New horizons, new hopes.
AU Wechsler B; Du L T; Piette J C
CS Internal Medicine Department, Pitie-Salpetriere Teaching Hospital, Paris, France.
SO REVUE DU RHUMATISME. ENGLISH EDITION, **(1998 Nov)** 65 (11) 619-24. Ref: 66
Journal code: 9313916. ISSN: 1169-8446.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990311
Last Updated on STN: 19990311
Entered Medline: 19990219

L8 ANSWER 7 OF 192 MEDLINE on STN
AN 1999046498 MEDLINE
DN 99046498 PubMed ID: 9829058
TI Antiphospholipid syndrome and pregnancy loss.
AU Rai R; Regan L
CS Department of Obstetrics and Gynaecology, Hillingdon Hospital, Uxbridge.
SO HOSPITAL MEDICINE, **(1998 Aug)** 59 (8) 637-9. Ref: 22
Journal code: 9803882. ISSN: 1462-3935.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals

EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981203
AB Antiphospholipid antibodies (aPL) are associated with recurrent miscarriage. Pregnancies that survive the first trimester risk developing **pre-eclampsia**, intrauterine growth retardation and fetal distress during labour. Pregnancy loss is initially caused by defective embryonic implantation and later by thrombosis of the placental vasculature. In women with aPL, thromboprophylaxis during pregnancy improves the live birth rate.

L8 ANSWER 8 OF 192 MEDLINE on STN
AN 1999010355 MEDLINE
DN 99010355 PubMed ID: 9793940
TI Ambulatory blood pressure monitoring in pregnancy.
AU Walker S P; Higgins J R; Brennecke S P
CS Department of Perinatal Medicine, Royal Women's Hospital, Melbourne, Australia.
SO OBSTETRICAL AND GYNECOLOGICAL SURVEY, **(1998 Oct)** 53 (10) 636-44.
Ref: 56
Journal code: 0401007. ISSN: 0029-7828.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981221
AB Hypertensive disorders of pregnancy remain a major cause of maternal and perinatal morbidity and mortality. **Diagnosis** and management of these disorders has relied on conventional blood pressure measurement, a technique fraught with error and uncertainty. Ambulatory blood pressure measurement is a promising new technique that has the potential to overcome the inaccuracies of conventional blood pressure measurement. Several ambulatory blood pressure monitors have been validated in pregnant populations, and normal reference ranges have been established. More recent research has focused on the potential clinical roles of ambulatory blood pressure measurement in pregnancy. This review addresses the limitations of conventional blood pressure measurement and reviews the current literature on the application of ambulatory blood pressure measurement in pregnancy.

L8 ANSWER 9 OF 192 MEDLINE on STN
AN 1999009959 MEDLINE
DN 99009959 PubMed ID: 9793564
TI Heart disease during pregnancy. Which cardiovascular changes are normal or transient?.
AU Villablanca A C
CS Division of Cardiovascular Medicine, University of California, School of Medicine, Davis 90272, USA.. avillablanca@ucdavis.edu
SO POSTGRADUATE MEDICINE, **(1998 Oct)** 104 (4) 183-4, 187-92. Ref: 10
Journal code: 0401147. ISSN: 0032-5481.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199811

ED Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981125

AB A normal, uncomplicated pregnancy causes many physiologic cardiovascular changes and symptoms. For example, maternal blood volume, heart rate, and cardiac output increase, and fatigue, orthopnea, and presyncope often occur. In general, these findings are innocuous. Physicians need to recognize those that are not typically associated with pregnancy, such as diastolic murmurs, paroxysmal nocturnal dyspnea, and syncope. **Diagnostic** evaluation of pregnant women must be approached cautiously to avoid risk to the fetus. Methods using ionizing radiation should be avoided whenever possible. Hypertension, one of the most common complications of pregnancy, may be transient and benign, or it may be chronic or gestational. Early recognition and intervention are beneficial to both the mother and the child.

L8 ANSWER 10 OF 192 MEDLINE on STN
AN 1998431305 MEDLINE
DN 98431305 PubMed ID: 9759141
TI Hypertension in pregnancy and preeclampsia--**diagnosis** and treatment.
AU Henriksen T
CS Department of Obstetrics and Gynecology, The National Hospital, Oslo, Norway.
SO SCANDINAVIAN JOURNAL OF RHEUMATOLOGY. SUPPLEMENT, **(1998)** 107 86-91. Ref: 13
Journal code: 0400360. ISSN: 0301-3847.
CY Norway
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199810
ED Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981021

AB Women who have or develop high blood pressure during pregnancy are all at increased risk of complications antenatally, intrapartum and in the puerperium. The increased risk applies to the mother as well to the fetus. Preeclampsia is the most serious form of hypertensive pregnancy complications. Preeclampsia is, however, not primarily a hypertensive disease but a disorder induced by factors dependent on the presence of placenta. The prime target of the placenta dependent factors is the vascular endothelium. Therefore the complications are associated with the vascular system, i.e. intravascular coagulation, bleeding and organ failure following poor perfusion. The fetus is at increased risk due to growth retardation and hypoxia following placental damage. Treatment of the hypertension is first indicated if the blood pressure rises to a level of increased risk of cerebral vascular complications, i.e. above 105-110 mmHg. Delivery is the only causal treatment and is always indicated if severe maternal or fetal complications develop.

=> d 11-20 bib ab

L8 ANSWER 11 OF 192 MEDLINE on STN
AN 1998428712 MEDLINE
DN 98428712 PubMed ID: 9732096
TI Liver problems in pregnancy: part 2--managing pre-existing and pregnancy-induced liver disease..
AU Everson G T
CS University of Colorado Health Sciences Center, Denver, USA.
SO MEDSCAPE WOMENS HEALTH, **(1998 Mar)** 3 (2) 2. Ref: 26

Journal code: 100844142. ISSN: 1521-2076.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Consumer Health
EM 199810
ED Entered STN: 19981020
Last Updated on STN: 19981020
Entered Medline: 19981008
AB In distinguishing normal from abnormal hepatic changes, the author described the expected changes in liver tests that occur during complicated pregnancy. This article reviews the forms of pre-existing liver disease that may affect or be affected by pregnancy, as well as liver diseases that tend to arise during pregnancy. Among the pre-existing liver diseases are autoimmune chronic active hepatitis, which may be activated by pregnancy and tends to be associated with an increased risk of still and premature births. Worsening of chronic hepatitis B and C has occasionally been observed. While some women with cirrhosis can sustain a normal pregnancy without any worsening of hepatic function, others develop liver failure; plus, women with cirrhosis are less fertile and have higher rates of both stillbirths and premature infants. Other liver disorders that may or may not be affected by pregnancy include Dubin-Johnson syndrome, Gilbert syndrome, benign recurrent intrahepatic cholestasis, Wilson's disease, hepatic adenomas, and focal nodular hyperplasia. Among the hepatic disorders that occur during pregnancy in normally healthy women and then resolve after delivery is intrahepatic cholestasis of pregnancy (also known as pruritus gravidarum, recurrent intrahepatic cholestasis of pregnancy, and obstetric hepatosis). Others include acute fatty liver of pregnancy and HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count), which may be part of the spectrum of disorders associated with **pre-eclampsia** /eclampsia. Pregnancy may also trigger the dissemination of herpes infection to the liver.

L8 ANSWER 12 OF 192 MEDLINE on STN
AN 1998348049 MEDLINE
DN 98348049 PubMed ID: 9684907
TI Pregnancy in chronic dialysis: a review and analysis of the literature.
AU Chan W S; Okun N; Kjellstrand C M
CS Department of Medicine, University of Alberta, Edmonton, Canada.
SO INTERNATIONAL JOURNAL OF ARTIFICIAL ORGANS, **(1998 May)** 21 (5) 259-68. Ref: 82
Journal code: 7802649. ISSN: 0391-3988.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199811
ED Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981103
AB Pregnancy is uncommon in end-stage renal failure, particularly in patients requiring dialysis. We reviewed the literature from 1965 to date, seeking an optimal way of dialyzing pregnant women after encountering one such patient METHODS: We searched the English literature by cross-referencing "pregnancy" with "hemo-" or "peritoneal dialysis" and "renal failure". Eighty-six pregnancies worldwide were found to which we added one case of our own. Various independent factors were studied against gestational age at delivery using uni- and multivariate analysis. These factors included mother's age, previous delivery, **diagnoses** of renal disease,

dialysis duration prior to pregnancy, gestational age at onset of dialysis, dialysis type, level of hemoglobin during pregnancy, BUN and creatinine targets, BUN/creatinine ratio, dialysis intensity at the beginning and end of pregnancy, influence of erythropoietin and dialysis complications. RESULTS: Of the 87 pregnancies, 12% resulted in stillbirths, 9% of neonates died prior to discharge. The mean gestational age at delivery was 32 +/- 5 weeks, and the mean birth weight 1604 +/- 652 g. Two congenital abnormalities and one twin pregnancy were reported. 48% of deliveries were premature. **Pre-eclampsia** was reported in 11%, and worsening hypertension in 17%. CAPD was used in 25 and hemodialysis in 62 patients. Fetal survival was similar in both cases (72% vs 82%), although incidence of various dialysis complications differed. The conventional dialysis goals of a low target BUN level and hemoglobin for pregnant patients were not factors in predicting fetal outcome. The number of hemodialyses/week were negatively correlated (R = -0.35, P = 0.061), but the hours of dialysis positively correlated (R = 0.42, p = 0.035) to gestational age. Fetal survival was independently influenced by creatinine level [564 micromol/L when baby survived vs 788 micromol/L when baby died (p = 0.021)], BUN/creatinine ratio (50 vs 30, p = 0.053), and hours of dialysis (5.6 hrs vs 3.6 hrs, p = 0.013). There was no relation of either frequency or volume of peritoneal dialysis exchanges to gestational age or fetal survival. CONCLUSIONS: Greater attention to a high intake of protein (>1.5 g/kg) and higher dose of hemodialysis, achieved by longer, every other day dialysis, may be the optimal approach to pregnant patients on hemodialysis. Our first attempt to define the goal of hemodialysis is to keep the predialysis creatinine below 600 mmol/L and the protein intake high enough so the predialysis BUN level is >25 mmol/L. There are no clear guidelines on how to best perform CAPD.

L8 ANSWER 13 OF 192 MEDLINE on STN
AN 1998243902 MEDLINE
DN 98243902 PubMed ID: 9583067
TI Hypertensive disorders of pregnancy. Differentiating preeclampsia from active systemic lupus erythematosus.
AU Repke J T
CS Department of Obstetrics and Gynecology, Harvard Medical School, Brigham and Women's Hospital, Boston, Massachusetts, USA.
SO JOURNAL OF REPRODUCTIVE MEDICINE, **(1998 Apr)** 43 (4) 350-4. Ref: 11
Journal code: 0173343. ISSN: 0024-7758.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980624
AB The **diagnosis** of preeclampsia is made on the basis of hypertension, proteinuria and edema. Unfortunately, all three of these findings can be seen in the patient who is experiencing a flare of systemic lupus erythematosus. The management of these conditions is entirely different. Preeclampsia frequently results in the need for delivery and occasionally, especially when remote from term, can result in significant neonatal morbidity and mortality. Systemic lupus may be treatable with a variety of pharmacologic agents. It is not always possible to make the distinction between active lupus and preeclampsia, and occasionally the two occur concurrently. Nevertheless, the goal of the rheumatologist and perinatologist is to try to make that distinction. Physical findings and serologic markers can be useful in helping to distinguish between these two **diagnoses**. Under certain

circumstances, delivery is indicated despite the presence of continued uncertainty as to the actual **diagnosis**.

L8 ANSWER 14 OF 192 MEDLINE on STN
AN 1998226312 MEDLINE
DN 98226312 PubMed ID: 9566660
TI Preeclampsia and cerebral palsy: are they related?.
AU Collins M; Paneth N
CS Department of Epidemiology, College of Human Medicine, Michigan State University, East Lansing 48824-1316, USA.
SO DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY, **(1998 Mar)** 40 (3) 207-11. Ref: 52
Journal code: 0006761. ISSN: 0012-1622.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW OF REPORTED CASES)
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980529
Last Updated on STN: 19980529
Entered Medline: 19980519

L8 ANSWER 15 OF 192 MEDLINE on STN
AN 1998220789 MEDLINE
DN 98220789 PubMed ID: 9562320
TI Neurological aspects of eclampsia.
AU Thomas S V
CS Department of Neurology, The Royal Hospital, Muscat, Sultanate of Oman.
SO JOURNAL OF THE NEUROLOGICAL SCIENCES, **(1998 Feb 18)** 155 (1) 37-43. Ref: 49
Journal code: 0375403. ISSN: 0022-510X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980828
Last Updated on STN: 19980828
Entered Medline: 19980818
AB Eclampsia accounts for a third of maternal mortality in developing countries. The neurological manifestations of eclampsia consist of seizures and alteration of sensorium or coma on a background of **pre-eclampsia**. Occasionally there can be focal neurological deficits too. Recent studies with CT scan and MRI have demonstrated the presence of cerebral edema and/or cerebral hemorrhage in eclampsia. EEG in patients with eclampsia has revealed evidence of diffuse cerebral dysfunction (delta waves) and epileptiform transients (spikes or sharp waves). There is also evidence of extensive vasculopathy within the brain parenchyma. A variety of mechanisms have been suggested to explain these changes, the most important being failure of autoregulation of cerebral blood flow that leads to cerebral edema and hemorrhage. There is considerable controversy regarding the treatment of seizures in eclampsia. Recent studies have shown that magnesium sulfate is superior to phenytoin or diazepam in the treatment of eclamptic seizures and prevention of eclamptic seizures in women with **pre-eclampsia**.

L8 ANSWER 16 OF 192 MEDLINE on STN
AN 1998220000 MEDLINE
DN 98220000 PubMed ID: 9559246

TI Systemic lupus erythematosus in pregnancy.
AU Duerbeck N B; Coney P J
CS Department of Obstetrics and Gynecology, Southern Illinois University School of Medicine, Springfield 62794-1617, USA.
SO COMPREHENSIVE THERAPY, **(1998 Mar)** 24 (3) 123-8. Ref: 28
Journal code: 7605837. ISSN: 0098-8243.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980611
Last Updated on STN: 19980611
Entered Medline: 19980602
AB Systemic lupus erythematosus is an inflammatory autoimmune disease that can affect multiple organ systems. The most popular theory regarding the origin of its clinical manifestations is that autoantibodies and circulating immune complexes become trapped in the capillaries of visceral structures.

L8 ANSWER 17 OF 192 MEDLINE on STN
AN 1998212673 MEDLINE
DN 98212673 PubMed ID: 9551309
TI Inherited thrombophilia and pregnancy.
AU Girling J; de Swiet M
CS West Middlesex Hospital, Isleworth, UK.
SO CURRENT OPINION IN OBSTETRICS AND GYNECOLOGY, **(1998 Apr)** 10 (2) 135-44. Ref: 67
Journal code: 9007264. ISSN: 1040-872X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980618
Last Updated on STN: 19980618
Entered Medline: 19980609
AB Inherited thrombophilia is associated with an increased risk of thrombosis. Classically it consists of protein C and protein S deficiency, activated protein C resistance and antithrombin III deficiency. In pregnancy, in addition to thrombosis, inherited thrombophilia is associated with poor obstetric outcome, including recurrent miscarriage, late fetal loss, abruption and **pre-eclampsia**. Hyperhomocysteinaemia is a newly recognized cause of familial thrombophilia. It is likely that further causes such as prothrombin gene mutations will be added to the rapidly expanding list. The **diagnosis** of some forms of genetic thrombophilia must, however, be approached with caution during pregnancy, particularly protein S deficiency and activated protein C resistance.

L8 ANSWER 18 OF 192 MEDLINE on STN
AN 1998212672 MEDLINE
DN 98212672 PubMed ID: 9551308
TI **Pre-eclampsia**--still a disease of theories?.
AU Higgins J R; Brennecke S P
CS Department of Perinatal Medicine, Royal Women's Hospital, Melbourne, Australia.
SO CURRENT OPINION IN OBSTETRICS AND GYNECOLOGY, **(1998 Apr)** 10 (2) 129-33. Ref: 42
Journal code: 9007264. ISSN: 1040-872X.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980618
Last Updated on STN: 19980618
Entered Medline: 19980609
AB The pathophysiology of **pre-eclampsia** remains poorly understood. Moreover, there is no reliable predictive test and no effective prophylactic therapy for this disease. Advances have, however, recently been made in our understanding of the genetics of **pre-eclampsia** and in the processes which lead to abnormal trophoblastic invasion in **pre-eclampsia**. Prediction and prevention are intimately linked, and both problems will only be solved by further unravelling of the complex pathophysiology of **pre-eclampsia**.

L8 ANSWER 19 OF 192 MEDLINE on STN
AN 1998205384 MEDLINE
DN 98205384 PubMed ID: 9543802
TI [Pregnancy, essential hypertension and chronic renal disease]. Graviditet, essensiell hypertensjon og kronisk nyresykdom.
AU Os I; Andersson K S; Oian P; Henriksen T
CS Nyremedisinsk avdeling, Ulleval sykehus, Oslo.
SO TIDSSKRIFT FOR DEN NORSKE LAEGEFORENING, **(1998 Feb 28)** 118 (6) 884-6. Ref: 40
Journal code: 0413423. ISSN: 0029-2001.
CY Norway
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Norwegian
FS Priority Journals
EM 199804
ED Entered STN: 19980430
Last Updated on STN: 19980430
Entered Medline: 19980417
AB Women with chronic hypertension or renal disease are at a particular high risk of developing **pre-eclampsia** or eclampsia. **Pre-eclampsia** is associated with an increased risk of fetomaternal complications. In women with uncomplicated mild and moderate hypertension, pregnancy is usually normal. Treatment of high blood pressure aims at reducing maternal cardio- and cerebrovascular catastrophies, and the benefit of the treatment must be weighed against possible harmful effects on the foetus. In some cases, antihypertensive treatment can be discontinued, or medication changed. Preconceptional counselling is important both for women with chronic hypertension and, even more so, for women with renal disease, since the outcome of the pregnancy may be affected by the underlying disease.

L8 ANSWER 20 OF 192 MEDLINE on STN
AN 1998139217 MEDLINE
DN 98139217 PubMed ID: 9527410
TI Hypertension in pregnancy.
AU Paller M S
CS University of Minnesota, Minneapolis 55455, USA.
SO JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, **(1998 Feb)** 9 (2) 314-21. Ref: 27
Journal code: 9013836. ISSN: 1046-6673.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980410
Last Updated on STN: 19980410
Entered Medline: 19980402

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---Logging off of STN---

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.54	12.75

STN INTERNATIONAL LOGOFF AT 17:31:44 ON 26 JUL 2003